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Resource Utilization and Direct Medical Costs of Chronic Hepatitis C in Thailand: A Heavy but Manageable Economic Burden

Satawat Thongsawat, MD[1,*], *Teerha Piratvisuth, MD*[2], *Chutima Pramoolsinsap, MD*[3], *Anuchit Chutaputti, MD*[4], *Tawesak Tanwandee, MD*[5], *Dittaya Thongsuk, MPH*[6]

[1]*Faculty of Medicine, Division of Gastronenterology, Department of Internal Medicine, Chiangmai University, Chiang Mai, Thailand;* [2]*Songklanagarind Hospital, Prince of Songkla University, Songkhla, Thailand;* [3]*Ramathibodi Hospital, Mahidol University, Bangkok, Thailand;* [4]*Phramongkutklao Hospital, Bangkok, Thailand;* [5]*Siriraj Hospital, Mahidol University, Bangkok, Thailand;* [6]*Roche Thailand Ltd., Bangkok, Thailand*

ABSTRACT

Objective: To estimate the cost for the management of chronic hepatitis C (CHC) and related morbidities by using a payer perspective in Thailand. **Methods:** Data elements were extracted from medical records of 542 patients newly diagnosed with CHC in five tertiary care hospitals across Thailand. All patients were divided into five health states: noncirrhotic CHC, hepatitis C virus (HCV)-related compensated cirrhosis, HCV-related decompensated cirrhosis, HCV-related hepatocellular carcinoma, and HCV-related liver transplantation. Resource utilization data for each patient during a 12-month follow-up study period were compiled, and reference prices published by the Thai government were used to estimate the cost for each health state. The average cost was calculated and categorized into various groups, for example, laboratory and diagnostic tests, procedures, medication, and hospitalization. **Results:** The average number of outpatient visits per patient was approximately six visits in all cohorts. The HCV-related hepatocellular carcinoma and liver transplantation cohorts had a higher average number of inpatient admissions per patient. The average number of days per admission varied from fewer than 3 days to 1 week or more across all the health states. The average annual total cost per patient varied across all health states from approximately 170,000 to 600,000 baht, and medication cost was the largest portion in every cohort, except the HCV-related liver transplantation cohort in year 1. Among all medications, the average annual antiviral medication cost per patient was the largest portion in the noncirrhotic CHC and HCV-related compensated cirrhosis cohorts. **Conclusions:** CHC was a costly disease in Thailand. The average annual medication cost was the largest portion in every health state, except HCV-related liver transplantation.

Keywords: direct medical cost, economic burden, hepatitis C virus, resource utilization.

Introduction

Hepatitis C virus (HCV) infection is a major disease burden on the world that affects 130 to 170 million people worldwide [1]. The disease can result in significant morbidities and mortality among infected patients. Seventy percent of HCV-infected patients will develop chronic infection [1]. Approximately 25% of these patients ultimately develop cirrhosis, and annually 1.6% of them develop hepatocellular carcinoma (HCC) [2–4]. Among the patients with cirrhosis, the annual rate of decompensation is about 4%, and its annual death rates are 15% and 30% in industrialized and developing countries, respectively [4]. For patients with HCC, the annual death rate depends on access to treatment and is estimated to be approximately 80% to 90% [4].

Currently, the standard treatment for chronic hepatitis C (CHC) is a combination of a weekly peginterferonalfa and daily oral ribavirin for approximately 1 year. The goal of CHC treatment is to have the highest overall sustained virological response rate [5–7]. Several factors including patient preferences, patient age, duration of infection, viral genotypes, HCV RNA levels, and presence of symptoms are considered when deciding whether or not to treat CHC. Generally, treatment is recommended for patients with moderate and severe CHC. In patients with a milder degree of disease, treatment is usually deferred and only monitoring of liver disease progression by biopsy at an interval of 4 to 5 years is required [8].

In Thailand, HCV infection is an important disease with a prevalence of approximately 1.8% across age groups and areas. The prevalence is higher in people older than 60 years (5%) and HIV-infected patients (7.8%) [9,10]. Given that CHC and its subsequent morbidities and mortality could result in a high burden on the country, understanding the economic implications of CHC and related morbidities is crucial for determining health policies on resource allocation. Because Thailand's health care system is

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* *Address correspondence to:* Satawat Thongsawat, Faculty of Medicine, Division of Gastronenterology, Department of Internal Medicine, Chiangmai University, 239 Huay Kaew Road, Muang District, Chiang Mai, Thailand 50200.

E-mail: satawat@yahoo.com.

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different from that of countries in which the data on economic burden from CHC are available, namely, in terms of practice styles, drug cost, payment systems, and population's characteristics, the country should have its own calculations. The data will not only have a profound impact on initial decision making but can also be used for further economic evaluation, for example, cost-effectiveness or cost-utility analysis. Therefore, this study was conducted with the objective to estimate the cost for the management of CHC and related morbidities by using a payer perspective in Thailand.

Methods

Study Design

This study was part of a retrospective and multicenter survey for resource utilization and outcomes in the management of patients with CHC and related morbidities in various health states in Thailand. Data on the real-world use of health care resources, including medications related to CHC and its complications per clinical discretion of the prescribing physician, were collected from the existing medical records. Because the majority of Thai people used public health care services, collecting data from public sector would be more meaningful to policymakers and payers, five major public tertiary care hospitals from urban and upcountry areas across Thailand were purposively recruited.

All patients who were newly diagnosed with CHC were identified by hepatologists at each study hospital during the study period (December 2007 through May 2008). The source of patient identification was the list of patients who were diagnosed with one of the five health states, namely, noncirrhotic CHC, HCV-related compensated cirrhosis, HCV-related decompensated cirrhosis, HCV-related HCC, and HCV-related liver transplantation, during the years 2003 to 2004. All medical records were reviewed before the beginning of data collection to ensure patients' eligibility criteria and completeness of the data.

The diagnostic criteria for CHC in this study were either positive results of anti-HCV from enzyme immunoassay or confirmatory testing (e.g., recombinant immunoblot assay) or positive results of HCV RNA from real-time polymerase chain reaction. Patients diagnosed with CHC but showing no evidence of cirrhosis were identified as noncirrhotic CHC cohort. Patients with HCV-related compensated cirrhosis were identified by biopsy, ultrasound, or some clinical signs, for example, portal hypertension, whereas patients with HCV-related decompensated cirrhosis were those who had the appearance of at least one episode of ascites, jaundice, encephalopathy, or variceal bleeding but did not show any evidence of HCC. Patients in the HCV-related HCC cohort were identified in accordance with HCC defined in the 2005 American Association for the Study of Liver Diseases practice guideline. Patients who had undergone HCV-related liver transplantation were classified into the HCV-related liver transplantation cohort. If there was a recent change in the patient's health state, the earliest health state was chosen to attain data of a single health state covering at least 12 months after diagnosis.

Eligible patients were required to have one of the five health states and to have available follow-up data for a 12-month period after the diagnosis of the health state, except for patients with HCC and liver transplantation in which the period of the available data could be less than 12 months. In addition, they had to have follow-up data in the specified period after being diagnosed with each health state (Fig. 1). Patients with noncirrhotic CHC and HCV-related

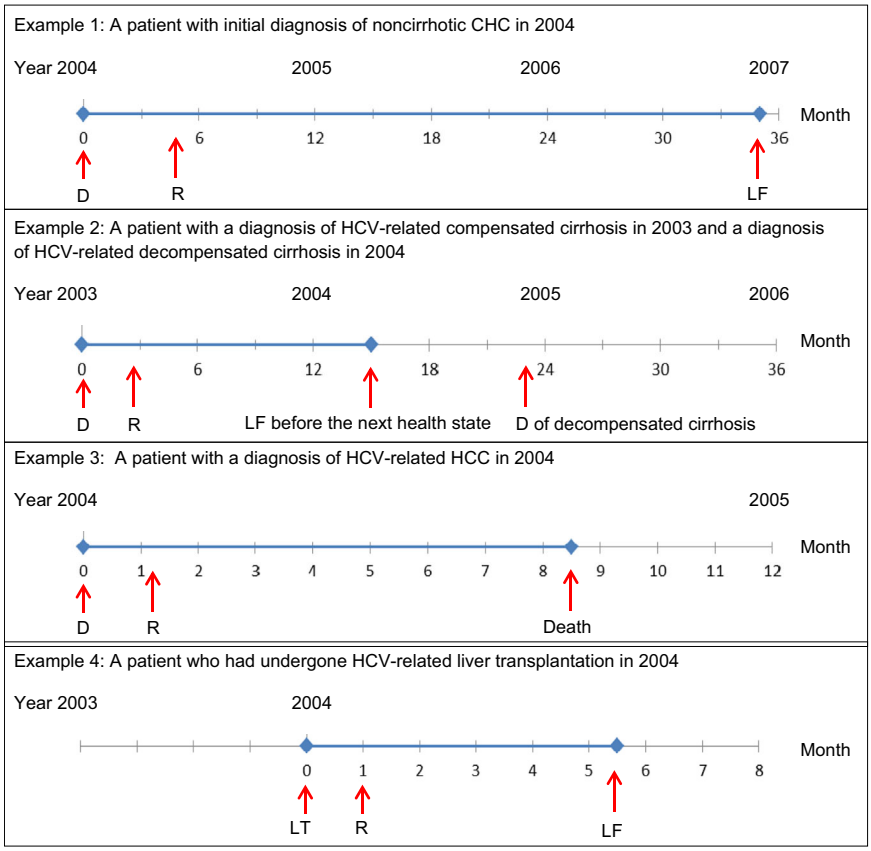

Fig. 1 – Examples for possible data collection periods (◆——◆). CHC, chronic hepatitis C; D, diagnosis; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; LF, last follow-up; LT, liver transplantation; R, revisit.

compensated cirrhosis had to have follow-up data within 6 months after diagnosis. Patients with HCV-related decompensated cirrhosis had to have follow-up data within 3 months after diagnosis. Patients with HCV-related HCC and HCV-related liver transplantation had to have follow-up data within 8 weeks after diagnosis or liver transplantation. These cutoffs were based on expert opinions that patients who had follow-up data later than the specified periods did not represent the normal practice pattern in Thailand and would confound resource utilization. The criteria excluded any patient who was involved in clinical trials or who had hepatitis B virus coinfection or who had clinical or known acute hepatitis A virus or hepatitis D virus infection or who had known human immunodeficiency virus or who had known medical conditions that were contraindicated to HCV treatment. A Web-based case report form was used for data collection. The data were collected from the time of initial diagnosis of a particular health state to the last follow-up visit or death.

Data Collection

The data were collected from patients' medical records. The use of these records was approved by each hospital's institution review board. Data on demographic characteristics, diagnosis dates, baseline characteristics, treatments and their outcomes, and resource utilization were extracted from the patients' medical records. The demographic data included patient's date of birth, sex, race, occupation, and payment type. Baseline characteristics included patient's weight, HCV genotype, fibrosis or cirrhosis, and comorbidities. Treatments included patient's medications, and their outcomes comprised sustained virological response, progression to cirrhosis, and progression to HCC. The resource utilization of this study included all medical-related resources, for example, diagnostic and laboratory tests, procedures, inpatient admission, outpatient visits, as well as medications for HCV treatment and related morbidities.

The diagnostic and laboratory test comprised a number of various tests in a year, for example, alanine aminotransferase, alkaline phosphatase, anti-HCV, and HCV viral load. Data on the number of procedures, for example, liver biopsy, computed tomography scan, magnetic resonance imaging, hemihepatectomy, and liver transplant, were collected. The inpatient admission data included the hospital admitted and discharged dates and the total number of admissions in a year. Data on the number of visits with general practitioners and gastroenterologists and to emergency room were collected from outpatient data. Data on the total amount of medications that patients obtained in a year, including both antiviral and other medications, were also compiled.

Statistical Analysis

All data were analyzed by using SAS, version 9.1.3 (SAS Institute, Inc., Cary, NC). Baseline patient characteristics were descriptively analyzed. All resource utilization data for each patient during the 12-month follow-up study period were compiled for each health state and on annual basis. The number of annual outpatient visits per patient, inpatient admissions per patient, and average length of stay days per admission were calculated to reflect the volume of utilization across the health states. Reference prices published by the Ministry of Public Health and the Ministry of Finance, Thailand, were used for estimating costs. These reference prices were a good measure for this study because the data were obtained from public hospitals. All the costs were adjusted to 2008 US dollar (35 Thai baht = US $1). Inflation adjustment to 2008 was performed on the basis of Thailand Consumer Price Index. The costs were stratified into laboratory and diagnostic tests, procedures, medication, and hospitalization for each health state.

Results

Patient characteristics across five HCV-related health states are shown in Table 1. A total of 542 patients were included in this study. Almost 55% of these patients were included in the noncirrhotic CHC cohort, while 25% of the recruited patients were diagnosed with HCV-related compensated cirrhosis. The rest of the patients or approximately 20% were in either the HCV-related decompensated cirrhosis cohort or the HCV-related HCC cohort. The proportion between male and female patients varied across all cohorts. Among all cohorts, the noncirrhotic CHC cohort was the youngest, with an average age of 49.4 years. Interestingly, patients covered by the Civil Servant Medical Benefit Scheme (CSMBS) and the state enterprise were the largest group in every cohort. Most of the patients' HCV genotype in this study was genotype 3, and a number of patients' genotypes were still unidentified, especially those of patients in the more severe health states. More than half of each cohort, except the HCV-related liver transplantation cohort, had no other comorbidity.

Table 2 shows the level of outpatient and inpatient utilizations across the health states. The average number of annual outpatient visits per patient among all cohorts was slightly different at around six to seven visits. For inpatient service, the HCV-related HCC and liver transplantation cohorts had significantly higher average number of inpatient admissions or hospitalizations (1–1.34 admissions) per patient than did other cohorts with less severe disease (0.08–0.35 admissions). While the average number of days that patients stayed in the hospital per admission was approximately fewer than 3 days for the noncirrhotic CHC and HCV-related compensated cirrhosis cohorts, the other cohorts on average stayed about 1 week or more per each admission.

Table 3 shows the average annual cost per patient for each resource category by each HCV-related health state. The average annual total cost per patient varied across all five health states from approximately US $4,900 to more than US $17,000. Among these health states, the HCV-related liver transplantation cohort had the highest average total annual cost per patient, particularly in year 1. The average annual total cost per patient of noncirrhotic CHC and HCV-related compensated cirrhosis cohorts was about the same but higher than that of HCV-related decompensated cirrhosis and HCC cohorts. The medication cost was the highest portion of the annual cost per patient in every cohort, and it declined while the health states became more severe, except the HCV-related liver transplantation cohort in year 1. There were two different sources of average annual medication cost among these health states. The average annual antiviral medication cost per patient of the noncirrhotic CHC and HCV-related compensated cirrhosis cohorts was much higher than their average annual cost per patient of other medications. In contrast, the HCV-related decompensated cirrhosis and HCC cohorts had lower average annual antiviral medication cost per patient, but their cost of other medications was higher. The HCV-related liver transplantation cohort in both their year 1 and later did not use the antiviral medications at all.

When the patients' health states became worse, the average annual procedure cost per patient tended to increase. It was especially high for the HCV-related HCC and liver transplantation cohorts. It should be noted that the average annual procedure cost per patient of the HCV-related liver transplantation cohort was tremendously high, and, in fact, higher than the other average total annual costs per patient. The average annual cost per patient for laboratory and diagnostic tests was not relatively high in all cohorts. The cost of laboratory and diagnostic tests, however, was highest for the HCV-related liver transplantation cohort. The average annual cost per patient of hospitalizations

Table 1 – Patient characteristics across HCV-related health states.

	Noncirrhotic CHC (N = 297; 54.80%)	Compensated cirrhosis (N = 136; 25.10%)	Decompensated cirrhosis (N = 64; 11.81%)	Hepatocellular carcinoma (N = 43; 7.93%)	Liver transplantation (N = 2; 0.37%)
Sex, n (%)					
Female	133 (44.8)	68 (50.0)	39 (60.9)	17 (39.5)	1 (50.0)
Male	164 (55.2)	68 (50.0)	25 (39.1)	26 (60.5)	1 (50.0)
Age (y), mean ± SD	49.4 ± 9.3	53.5 ± 8.8	54.6 ± 12.8	58.1 ± 8.9	56.0 ± 8.9
Reimbursement scheme, n (%)					
CSMBS	211 (71.2)	73 (53.9)	29 (44.6)	22 (50.0)	2 (100)
UC Scheme	13 (4.3)	28 (20.6)	19 (30.8)	11 (27.3)	0
SSS	9 (3.0)	2 (1.4)	0	2 (4.5)	0
Self-pay	58 (19.5)	32 (23.4)	16 (24.6)	7 (15.9)	0
Others	6 (2.0)	1 (0.7)	0	1 (2.3)	0
Genotype					
Genotype 1	128 (43.1)	33 (24.3)	11 (17.2)	7 (16.3)	0
Genotype 3	148 (49.8)	85 (62.5)	12 (18.8)	6 (14.0)	1 (50)
Others	5 (1.7)	0	0	1 (2.3)	0
NI	16 (5.4)	18 (13.2)	41 (64.1)	29 (67.4)	1 (50)
No. of comorbidities					
0	188 (63.3)	73 (53.7)	42 (65.6)	27 (62.8)	0
1	66 (22.2)	38 (27.9)	12 (18.7)	8 (18.6)	1 (50)
2	34 (11.4)	17 (12.5)	6 (9.4)	8 (18.6)	1 (50)
3	7 (2.4)	6 (4.4)	3 (4.7)	0	0
4	2 (0.7)	2 (1.5)	1 (1.6)	0	0

CHC, chronic hepatitis C; CSMBS, Civil Servant Medical Benefit Scheme; HCV, hepatitis C virus; NI, not identified; SSS, Social Security Scheme; UC, Universal Coverage.

was the lowest cost when compared with the other costs in every health state, and its amount increased when the health states became worse.

Discussion

This study was the first estimation of a direct economic burden of CHC on Thailand. Almost 80% of the patients were found in the first two less severe states, which were the noncirrhotic CHC and HCV-related compensated cirrhosis cohorts. This finding was correlated with the nature of CHC disease [2–4]. The noncirrhotic CHC cohort was slightly younger than the other cohorts, and the average age tended to be higher in the more severe health states. This result was consistent with the natural history of HCV infection, which is age-dependent, and the older age at infection was associated with the increased rate of fibrosis progression [1,11]. For reimbursement schemes, there are three public health insurance schemes in Thailand, including the CSMBS for all government employees, dependents, government retirees, and state enterprise employees; the Social Security Scheme (SSS) for private sector employees; and the Universal Coverage Scheme for

Table 2 – Annual utilization of outpatient and inpatient hospital services per patient across HCV-related health states.

	Noncirrhotic CHC (N = 297)	Compensated cirrhosis (N = 136)	Decompensated cirrhosis (N = 64)	Hepatocellular carcinoma (N = 43)	Liver transplantation (N = 2)	
					Year 1	Year 2+
Average number of OP visits per patient	6.56 ± 2.42	6.33 ± 2.43	6.21 ± 2.24	7.07 ± 3.84	6.50 ± 3.54	6.25 ± 2.47
Average number of IP admissions per patient	0.10 ± 0.20	0.08 ± 0.24	0.35 ± 0.70	1.34 ± 1.56	1.00 ± –	–
Average length of stay per admission (d)	1.01 ± 0.93	2.57 ± 2.03	8.69 ± 16.32	6.21 ± 5.44	15.50 ± 4.95	–

Note. Values are mean ± SD.
CHC, chronic hepatitis C; HCV, hepatitis C virus; IP, inpatient; OP, outpatient.

Table 3 – Average annual cost (2008 US $) per patient by HCV-related health states and resource categories.

Resource category	Noncirrhotic CHC (N = 297)	Compensated cirrhosis (N = 136)	Decompensated cirrhosis (N = 64)	Hepatocellular carcinoma (N = 43)	Liver transplantation (N = 2)	
					Year 1	Year 2+
Laboratory and diagnostic tests	263.23 ± 124.66	274.68 ± 146.17	220.73 ± 192.31	191.93 ± 97.76	784.21 ± 602.59	442.81 ± 121.08
Procedures	12.10 ± 37.69	53.78 ± 141.80	235.99 ± 440.50	1,052.79 ± 1,043.18	12,664.33 ± 439.36	–
Medications	7,550.53 ± 5,589.67	7,354.49 ± 6,010.83	4,456.80 ± 7,585.34	3,525.62 ± 5,708.43	3,681.12 ± 1,428.97	2,354.47 ± 56.95
Antiviral medications	6,005.60 ± 7,883.75	5,644.73 ± 6,827.69	1,117.61 ± 5,188.28	199.38 ± 917.94	–	–
Other medications	1,344.08 ± 2,471.34	2,028.13 ± 3,014.76	3,465.34 ± 4,875.05	2,940.00 ± 5,226.83	3,681.12 ± 1,428.97	2,354.47 ± 56.95
Hospitalizations	1.56 ± 5.42	2.65 ± 9.23	38.16 ± 102.39	116.81 ± 165.77	204.66 ± 62.95	–
Total	7,827.42 ± 5,670.87	7,685.60 ± 6,107.51	4,951.68 ± 7,782.85	4,887.14 ± 5,638.09	17,334.32 ± 1,655.16	2,797.28 ± 178.03

Note. Values represent mean ± SD.
CHC, chronic hepatitis C; HCV, hepatitis C virus.

the rest of the population not covered by the CSMBS or the SSS. CSMBS beneficiaries were the largest group of the patients in every cohort of this study, which was inconsistent with the fact that the Universal Coverage Scheme was the largest public insurance with 75% of population coverage while the SSS and the CSMBS covered only 15% and 8% of the Thai population, respectively. A reason could be that the payment type of the CSMBS was fee for service while the other schemes used capitation payment. All medical costs could be reimbursed for the CSMBS, which allowed CSMBS beneficiaries to access more health care services, particularly in tertiary care hospitals where this study was conducted. This study also identified the patients' HCV genotypes, and the results showed that the genotypes were consistent with previous epidemiology studies in Thailand, which indicated that the most prevalent genotype of HCV among the Thai population was genotype 3 [12,13]. This confirmed that the prevalence of the HCV genotype in Thailand is different from that in other Southeast Asian countries, in which the majority of the HCV genotype was type 1 [14]. Overall, most patient characteristics of this study were consistent with the nature of CHC disease and epidemiology in Thailand. So, the selection conditions had little effect on the representativeness of the patient sample.

The similar annual numbers of outpatient visits per patient across all cohorts indicated that no matter how severe the CHC was, the patients on average saw their doctors every 2 months. Severity, however, seemed to be a good explanation of other results of resource utilization. Less severe patients, including the noncirrhotic CHC, HCV-related compensated cirrhosis, and HCV-related decompensated cirrhosis cohorts, were admitted to hospitals less often and tended to stay in the hospital shorter than did more severe patients, including the HCV-related HCC and liver transplantation cohorts. No previous study reported resource utilization of each HCV-related health state. The results of each health state in this study, however, were not largely different from the results of a recent study in the United States, which revealed that the overall chronic HCV average number of annual hospital admissions and annual inpatient days was 0.46 times and 7.74 days, respectively [15].

The average annual total direct cost per patient for every cohort in this study enormously exceeded that of some health conditions in Thailand such as diabetes (approximately US $185.71) and road traffic injuries (approximately US $94.29) [16,17]. These results indicated that the direct economic burden of CHC was very high and demanded policymakers' attentions. The HCV-related liver transplantation cohort had the highest average annual total cost per patient driven by the cost of medical procedures. The cost of medications was a major component driving the overall total cost of patients with CHC. Basically, the goal of CHC treatment is to prevent complications of HCV infection [8]. Thai hepatologists recommended that HCV-infected patients, who are in the noncirrhotic CHC with abnormal alanine aminotransferase and HCV-related compensated cirrhosis cohorts, should be treated by antiviral medications, for example, peginterferon and ribavirin [18]. The cost of these antiviral medications was relatively high, and their treatment periods were long. Undoubtedly, they were the major cost of the first two cohorts. The proportions of these antiviral medication cost to the overall cost, which was approximately more than 90%, were similar to those of two studies in the United States [19,20]. Other medications played more important roles in HCV-related decompensated cirrhosis, HCV-related HCC, and HCV-related liver transplantation. Thai hepatologists suggested considering liver transplantation, instead of antiviral treatments, for the HCV-related decompensated cirrhosis cohort [18]. This might explain why the average annual antiviral medication cost dropped considerably in this cohort. Similarly, the average

annual cost of antiviral medications in the HCV-related HCC and liver transplantation cohorts was very low while the cost of other medications went up.

Various laboratory and diagnosis tests for monitoring patients' responses to antiviral medications were recommended. Moreover, periodic liver biopsies were recommended for patients in these two health states who might be unwilling to undergo antiviral treatments [21]. These contributed to the relatively higher average annual laboratory and diagnostic test cost for noncirrhotic CHC and HCV-related compensated cirrhosis cohorts compared with those of HCV-related decompensated cirrhosis and HCC cohorts.

The average annual procedure cost per patient increased when the health states became more severe. Its amounts were higher than the average annual total cost of every cohort, and thus the HCV-related liver transplantation cohort had the highest average annual total cost per patient. Even though the sample size of this cohort was very small, the relatively high cost of liver transplantation should be brought to policymakers' attention. Policymakers needed to consider a trade-off between providing expensive antiviral medications to patients newly diagnosed with noncirrhotic CHC or HCV-related compensated cirrhosis and saving antiviral costs but taking future risks of patients progressing to more severe disease stages, which might lead to higher costs from liver transplantation or patient's death.

The average annual cost of hospitalization per patient was the lowest when compared with other costs in every health state. This result was inconsistent with results from a study conducted in the United States, which indicated that hospitalization was one of the key cost drivers [15]. This finding, however, was reasonable because the hospitalization cost in Thailand was much lower than in the United States due to the lower labor cost. The increases in average annual hospitalization cost per patient in more severe health states were concordant with the inpatient service utilization shown in Table 2 that patients in later health states tended to have a higher number of inpatient admissions and longer length of stays.

There were several limitations to this study. First, the retrospective study design could result in incomplete data. Retrospective study design, however, was considered the most appropriate due to the time and budget limitations. Second, the small sample size, especially the HCV-related liver transplantation cohort, could cause some biases. This might reflect, however, the real situation in Thailand in which few patients underwent liver transplantation because of both clinical and financial reasons. Third, the generalizability of study results might be limited. Because Thailand's health care system, economic structure, and CHC patient characteristics differ from those of many other countries, these factors should be considered in generalizing and applying the results to other countries because resource utilization for CHC and related morbidities depended very much on these factors. In addition, all patients in this study were from tertiary care hospitals, which were usually well equipped with technology and experts. The decision on treatments and/or other tests in provincial hospitals, district hospitals, or primary health care units could be different from those in these high-level hospitals. Fourth, the medical cost in this study was not specific only to CHC disease due to possible confounding factors from patients' other comorbidities. The majority of the patients in every cohort, except the HCV-related liver transplantation cohort, had no other comorbidities during the data collection periods. Fifth, the study collected data only from patients newly diagnosed with CHC and related morbidities. The costs and resource utilization could have been different if we had included data from patients with related morbidities progressing from CHC. Finally, all costs in this study were estimated from reference prices established by the Ministry of Public Health and the Ministry of Finance. The reference prices suited the study perspective, but they might or might not have reflected real-world unit prices. They were the best estimation, however, unless the microcosting method, which would require large amount of resources, was used.

Conclusions

This study showed that CHC was one of the costly diseases in Thailand, and it could become more costly if liver cirrhosis developed and eventually required liver transplantation. Despite some limitations, the study generated interesting points to policymakers and payers that early proper CHC treatment might help to prevent more costs as the disease progresses to more advanced stages. Future research should focus on not only amending the study limitations but also extending the study results. Indirect costs attributable to any HCV-related health states should be investigated to capture the societal perspective of the CHC treatments. A full economic evaluation of antiviral medications, for example, cost-effectiveness analysis, and their budget impact analysis for the country were also recommended.

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